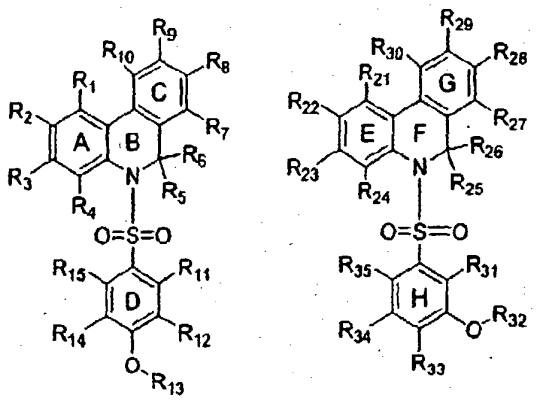
10/718,461

Filed 9-7-04

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (original) A compound of formulae (I) or (II) having the structure



(I)

(II)

Cancel 15-18, make 11-14 and 19 depend on 10

wherein

R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{14}, and R_{15} are each, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-S(O)$_2$-, R_{17}-SO_3-, R_{17}-S(O)$_2$NR-, -N(R)$_2$, -NR-C(NH$_2$)=NR, cyano, nitro, halogen, -OR, -SR, -SO_3R, -S(O)$_2$N(R)$_2$, -C(O)R, -C(R)=N-OR, -C(NH$_2$)=NR, -CO_2R, -OC(O)R, or -C(O)N(R)$_2$; or are taken together with either R_{p+1} or R_{p-1} linked with an -alkylene-, or -X-alkylene- group;

Two adjacent groups

an adjacent

-X-A

R_5 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -C(O)N(R)$_2$; or R_5 may be taken together with either R_6 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_6 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -C(O)N(R)$_2$; or R_6

may be taken together with either R_5 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_{13} is R, R_{17}-X-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, -SO_3R, -$S(O)_2N(R)_2$, or D-glucuronidate;

R_{16} is -alkylene-, -cycloalkylene-, -alkylene-X-alkylene-, -alkylene-X-cycloalkylene-, -cycloalkylene-X-alkylene-, or -cycloalkylene-X-cycloalkylene-;

R_{17} is alkyl, aryl, heteroaryl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, alkenyl-X-alkylene-, cycloalkenyl-X-alkylene-, or perfluoroalkyl;

R is, independently, hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, monofluoroalkyl, perfluoroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, hydroxy-(C_2-C_6)alkyl, alkoxyalkyl, alkylthioalkyl, formyl, acyl, alkoxycarbonyl, -$C(O)NH_2$, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminoalkyl, or dialkylaminoalkyl; or when an atom contains two R groups, the R groups may be taken together linked with an -alkylene- group;

X is O, -NR-, -$S(O)_m$-, -C(O)-, -OC(O)-, -C(O)O-, -NRC(O)-, or -C(O)NR-;

m is 0, 1, or 2;

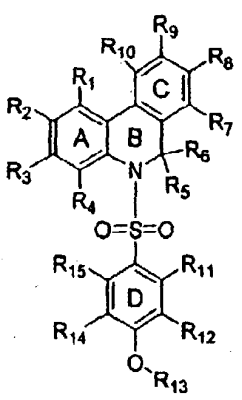
p is 2, 3, 6, 7, 8, 9, 12, 13, or 14;

R_{21}, R_{22}, R_{23}, R_{24}, R_{27}, R_{28}, R_{29}, R_{30}, R_{31}, R_{33}, R_{34}, and R_{35} are, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, R_{17}-SO_3-, R_{17}-$S(O)_2NR$-, -$N(R)_2$, -NR-$C(NH_2)$=NR, cyano, nitro, halogen, -OR, -SR, -SO_3R, -$S(O)_2N(R)_2$, -C(O)R, -C(R)=N-OR, -$C(NH_2)$=NR, -CO_2R, -OC(O)R, or -C(O)$N(R)_2$; or are taken together with either R_{q+1} or R_{q-1} linked with an -alkylene-, or -Y-alkylene- group;

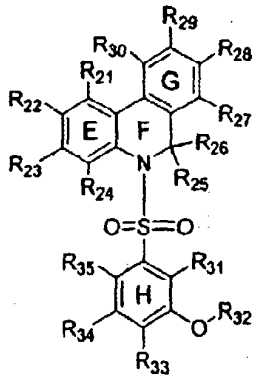
R_{25} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -C(O)$N(R)_2$; or R_{25} may be taken together with either R_{26} or R_{27} and linked with an -alkylene- or -Y-alkylene- group;

R_{26} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -C(O)$N(R)_2$; or R_{26} may be taken together with either R_{25} or R_{27} and linked with an -alkylene- or -Y-alkylene- group;

R_{32} is R, R_{17}-Y-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, -SO_3R, -$S(O)_2N(R)_2$, or D-glucuronidate;



(I)



(II)

wherein

R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{14}, and R_{15} are each, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-S(O)$_2$-, R_{17}-SO$_3$-, R_{17}-S(O)$_2$NR-, -N(R)$_2$, -NR-C(NH$_2$)=NR, cyano, nitro, halogen, -OR, -SR, -SO$_3$R, -S(O)$_2$N(R)$_2$, -C(O)R, -C(R)=N-OR, -C(NH$_2$)=NR, -CO$_2$R, -OC(O)R, or -C(O)N(R)$_2$; or are taken together with either an adjacent R_{p+1} or R_{p-1} linked with an -alkylene-, or -X-alkylene- group;

EX-A

R_5 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, -CR(O), -CO$_2$R, or -C(O)N(R)$_2$; or R_5 may be taken together with either R_6 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_6 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, -CR(O), -CO$_2$R, or -C(O)N(R)$_2$; or R_6 may be taken together with either R_5 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_{13} is R, R_{17}-X-R_{16}-, R_{17}-S(O)-, R_{17}-S(O)$_2$-, -SO$_3$R, -S(O)$_2$N(R)$_2$, or D-glucuronidate;

R_{16} is -alkylene-, -cycloalkylene-, -alkylene-X-alkylene-, -alkylene-X-cycloalkylene-, -cycloalkylene-X-alkylene-, or -cycloalkylene-X-cycloalkylene-;

R_{17} is alkyl, aryl, heteroaryl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, alkenyl-X-alkylene-, cycloalkenyl-X-alkylene-, or perfluoroalkyl;

R is, independently, hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, monofluoroalkyl, perfluoroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, hydroxy-(C_2-C_6)alkyl, alkoxyalkyl, alkylthioalkyl, formyl, acyl, alkoxycarbonyl, -$C(O)NH_2$, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminoalkyl, or dialkylaminoalkyl; or when an atom contains two R groups, the R groups may be taken together linked with an -alkylene- group;

X is O, -NR-, -$S(O)_m$-, -C(O)-, -OC(O)-, -C(O)O-, -NRC(O)-, or -C(O)NR-;

m is 0, 1, or 2;

p is 2, 3, 6, 7, 8, 9, 12, 13, or 14;

R_{21}, R_{22}, R_{23}, R_{24}, R_{27}, R_{28}, R_{29}, R_{30}, R_{31}, R_{33}, R_{34}, and R_{35} are, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, R_{17}-SO_3-, R_{17}-$S(O)_2NR$-, -$N(R)_2$, -NR-$C(NH_2)$=NR, cyano, nitro, halogen, -OR, -SR, -SO_3R, -$S(O)_2N(R)_2$, -C(O)R, -C(R)=N-OR, -$C(NH_2)$=NR, -CO_2R, -OC(O)R, or -$C(O)N(R)_2$; or are taken together with either an adjacent R_{q+1} or R_{q-1} linked with an -alkylene-, or -Y-alkylene- group;

FX-A

R_{25} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -$C(O)N(R)_2$; or R_{25} may be taken together with either R_{26} or R_{27} and linked with an -alkylene- or -Y-alkylene- group;

R_{26} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -$C(O)N(R)_2$; or R_{26} may be taken together with either R_{25} or R_{27} and linked with an -alkylene- or -Y-alkylene- group;

R_{32} is R, R_{17}-Y-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, -SO_3R, -$S(O)_2N(R)_2$, or D-glucuronidate;

Y is O, -NR-, -$S(O)_n$-, -C(O)-, -OC(O)-, -C(O)O-, -NRC(O)-, or -C(O)NR-;

n is 0, 1, or 2;

q is 22, 23, 26, 27, 28, 29, 32, 33, or 34;

or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

10. (currently amended) A method of treating ~~or inhibiting~~ chronic inflammatory disease in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.

claim 10 wherein the said disease is

11. (currently amended) A method of ~~treating or inhibiting~~ rheumatoid arthritis, spondyloarthropathies, osteoarthritis, psoriatic arthritis, or juvenile arthritis ~~in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.~~

claim 10 wherein the said disease is

12. (currently amended) A method of ~~treating or inhibiting~~ inflammatory bowel disease, Crohn's disease, ulcerative colitis, or indeterminate colitis ~~in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.~~

claim 10 wherein the said disease is

13. (currently amended) A method of ~~treating or inhibiting~~ psoriasis ~~in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1~~.

claim 10 wherein the said disease is

14. (currently amended) A method of ~~treating or inhibiting~~ asthma or chronic obstructive pulmonary disease ~~in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.~~

15. (currently amended) A method of treating ~~or inhibiting~~ stroke, ischemia, or reperfusion injury in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.

16. (currently amended) A method of lowering cholesterol, triglycerides, Lp(a), and LDL levels; ~~inhibiting or~~ treating hypercholesteremia, hyperlipidemia, cardiovascular disease, atherosclerosis, acute coronary syndrome, peripheral vascular disease, restenosis, or vasospasm in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.

17. (currently amended) A method of treating ~~or inhibiting~~ Alzheimer's disease, cognitive decline, of senile dementia in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.

18. (currently amended) A method of treating ~~or inhibiting~~ type II diabetes in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1.

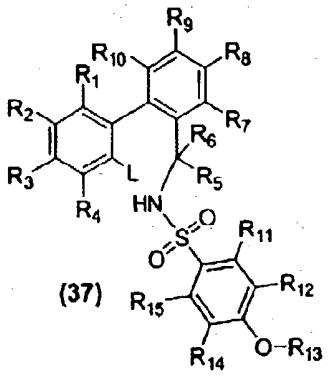
claim 16 wherein the said disease is

19. (currently amended) A method of ~~treating or inhibiting~~ sepsis ~~in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of claim 1~~.

20. (new) The compound according to claim 2, wherein R_{13} is $-S(O)_2NH_2$, or a pharmaceutically acceptable salt thereof.

21. (new) The compound according to claim 5, wherein R_{32} is $-S(O)_2NH_2$, or a pharmaceutically acceptable salt thereof.

22. (new) A process comprising providing a sulfonamide of formula 37:



(37)

wherein

R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{14}, and R_{15} are each, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl,

$HO-R_{16}$-, R_{17}-X-R_{16}-, $HS-R_{16}$-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, R_{17}-SO_3-, R_{17}-$S(O)_2NR$-, -$N(R)_2$, -NR-$C(NH_2)$=NR, cyano, nitro, halogen, -OR, -SR, -SO_3R, -$S(O)_2N(R)_2$, -C(O)R, -C(R)=N-OR, -$C(NH_2)$=NR, -CO_2R, -OC(O)R, or -$C(O)N(R)_2$; or are taken together with either an adjacent R_{p+1} or R_{p-1} linked with an -alkylene-, or -X-alkylene- group;

EXT

R_5 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, $HS-R_{16}$-, -CR(O), -CO_2R, or -$C(O)N(R)_2$; or R_5 may be taken together with either R_6 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_6 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, $HS-R_{16}$-, -CR(O), -CO_2R, or -$C(O)N(R)_2$; or R_6 may be taken together with either R_5 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_{13} is R, R_{17}-X-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, -SO_3R, -$S(O)_2N(R)_2$, or D-glucuronidate;

R_{16} is -alkylene-, -cycloalkylene-, -alkylene-X-alkylene-, -alkylene-X-cycloalkylene-, -cycloalkylene-X-alkylene-, or -cycloalkylene-X-cycloalkylene-;

R_{17} is alkyl, aryl, heteroaryl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, alkenyl-X-alkylene-, cycloalkenyl-X-alkylene-, or perfluoroalkyl;

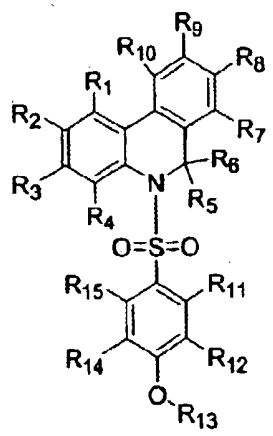
R is, indcpendently, hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, monofluoroalkyl, perfluoroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, hydroxy-(C_2-C_6)alkyl, alkoxyalkyl, alkylthioalkyl, formyl, acyl, alkoxycarbonyl, -$C(O)NH_2$, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminoalkyl, or dialkylaminoalkyl; or when an atom contains two R groups, the R groups may be taken together linked with an -alkylene- group;

X is O, -NR-, -$S(O)_m$-, -C(O)-, -OC(O)-, -C(O)O-, -NRC(O)-, or -C(O)NR-;

m is 0, 1, or 2; and

p is 2, 3, 6, 7, 8, 9, 12, 13, or 14; and

treating the sulfonamide of formula 37 with potassium carbonate to produce a phenanthridine of formula I:



(I)

wherein

R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{14}, and R_{15} are each, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-S(O)$_2$-, R_{17}-SO$_3$-, R_{17}-S(O)$_2$NR-, -N(R)$_2$, -NR-C(NH$_2$)=NR, cyano, nitro, halogen, -OR, -SR, -SO$_3$R, -S(O)$_2$N(R)$_2$, -C(O)R, -C(R)=N-OR, -C(NH$_2$)=NR, -CO$_2$R, -OC(O)R, or -C(O)N(R)$_2$; or are taken together with either R_{p+1} or R_{p-1} linked with an -alkylene-, or -X-alkylene- group;

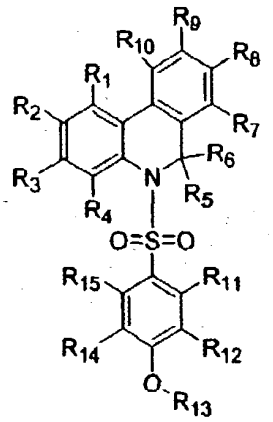
Ex. A

R_5 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, -CR(O), -CO$_2$R, or -C(O)N(R)$_2$; or R_5 may be taken together with either R_6 or R_7 and linked with an -alkylene- or -X-alkylene- group;

R_6 is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-X-R_{16}-, HS-R_{16}-, -CR(O), -CO$_2$R, or -C(O)N(R)$_2$; or R_6 may be taken together with either R_5 or R_7 and linked with an -alkylene- or -X-alkylene- group;

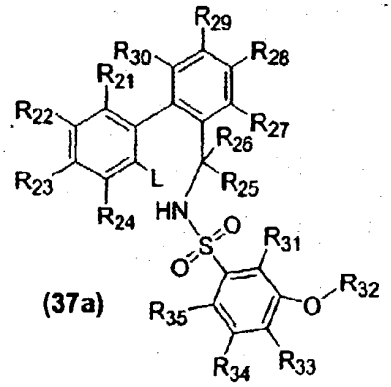
R_{13} is R, R_{17}-X-R_{16}-, R_{17}-S(O)-, R_{17}-S(O)$_2$-, -SO$_3$R, -S(O)$_2$N(R)$_2$, or D-glucuronidate;

R_{16} is -alkylene-, -cycloalkylene-, -alkylene-X-alkylene-, -alkylene-X-cycloalkylene-, -cycloalkylene-X-alkylene-, or -cycloalkylene-X-cycloalkylene-;



(I)

28. (new) A process comprising providing a sulfonamide of formula 37a:



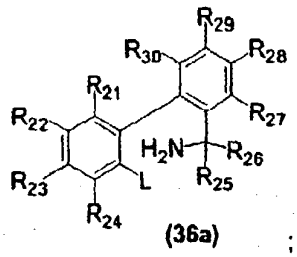
(37a)

wherein

R_{21}, R_{22}, R_{23}, R_{24}, R_{27}, R_{28}, R_{29}, R_{30}, R_{31}, R_{33}, R_{34}, and R_{35} are, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-S(O)$_2$-, R_{17}-SO_3-, R_{17}-S(O)$_2$NR-, -N(R)$_2$, -NR-C(NH_2)=NR, cyano, nitro, halogen, -OR, -SR, -SO_3R, -S(O)$_2$N(R)$_2$, -C(O)R, -C(R)=N-OR, -C(NH_2)=NR, -CO_2R, -OC(O)R, or -C(O)N(R)$_2$; or are taken together with either R_{q+1} or R_{q-1} linked with an -alkylene-, or -Y-alkylene- group;

R_{25} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -C(O)N(R)$_2$; or R_{25}

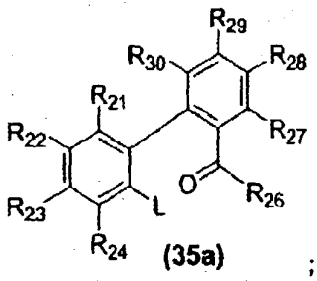
30. (new) The process of claim 29 further comprising providing a biphenylamine of formula 36a:



(36a) ; and

separating the biphenylamine of formula 36a into its respective enantiomers.

31. (new) The process of claim 30 further comprising providing a compound of formula 35a:

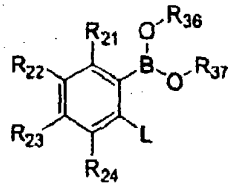


(35a) ;

reacting the compound of formula 35a with an ammonium source optionally in the presence of an acid catalyst to produce an intermediate imine; and

reducing the intermediate imine with a hydride source to produce a biphenylamine of formula 36a.

32. (new) The process of claim 31 further comprising providing a compound of formula 33a:

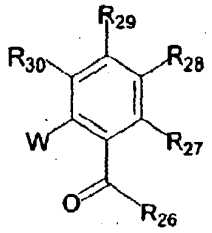


(33a)

wherein

R_{36} and R_{37} are, independently, hydrogen or (C_1-C_4) lower straight chain or (C_3-C_6) branched chain alkyl, or R_{36} and R_{37} are taken together to form a pinacol moiety; and

reacting the compound of formula 33a in the presence of a coupling catalyst with a compound of formula 34a:



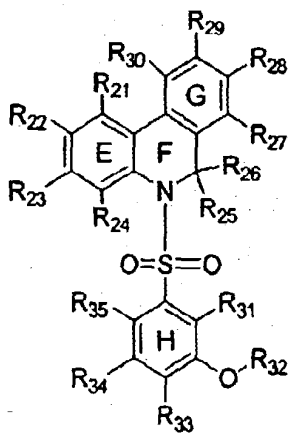
(34a)

wherein

W is a chlorine, bromine, or iodine atom, or a triflate ($-OSO_2CF_3$) moiety;

to produce a compound of formula 35. 35a

33. (new) A process for preparing a compound of formula II:



(II)

wherein

R_{21}, R_{22}, R_{23}, R_{24}, R_{27}, R_{28}, R_{29}, R_{30}, R_{31}, R_{33}, R_{34}, and R_{35} are, independently, hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, R_{17}-SO_3-, R_{17}-$S(O)_2NR$-, -$N(R)_2$, -NR-$C(NH_2)$=NR, cyano, nitro, halogen, -OR, -SR, -SO_3R, -$S(O)_2N(R)_2$, -C(O)R, -C(R)=N-OR, -$C(NH_2)$=NR, -CO_2R, -OC(O)R, or -$C(O)N(R)_2$; or are taken together with either R_{q+1} or R_{q-1} linked with an -alkylene-, or -Y-alkylene- group;

Ex A

Gradient

R_{25} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -$C(O)N(R)_2$; or R_{25} may be taken together with either R_{26} or R_{27} and linked with an -alkylene- or -Y-alkylene- group;

R_{26} is hydrogen, R_{17}, monofluoroalkyl, monofluoroalkenyl, aryl-R_{16}-, heteroaryl-R_{16}-, hydroxyalkyl, HO-R_{16}-, R_{17}-Y-R_{16}-, HS-R_{16}-, -CR(O), -CO_2R, or -$C(O)N(R)_2$; or R_{26} may be taken together with either R_{25} or R_{27} and linked with an -alkylene- or -Y-alkylene- group;

R_{32} is R, R_{17}-Y-R_{16}-, R_{17}-S(O)-, R_{17}-$S(O)_2$-, -SO_3R, -$S(O)_2N(R)_2$, or D-glucuronidate;

R_{16} is -alkylene-, -cycloalkylene-, -alkylene-X-alkylene-, -alkylene-X-cycloalkylene-, -cycloalkylene-X-alkylene-, or -cycloalkylene-X-cycloalkylene-;

R_{17} is alkyl, aryl, heteroaryl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, alkenyl-X-alkylene-, cycloalkenyl-X-alkylene-, or perfluoroalkyl;

R is, independently, hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, monofluoroalkyl, perfluoroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, hydroxy-(C_2-C_6)alkyl, alkoxyalkyl, alkylthioalkyl, formyl, acyl, alkoxycarbonyl, -$C(O)NH_2$, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminoalkyl, or dialkylaminoalkyl; or when an atom contains two R groups, the R groups may be taken together linked with an -alkylene- group;

Y is O, -NR-, -$S(O)_n$-, -C(O)-, -OC(O)-, -C(O)O-, -NRC(O)-, or -C(O)NR-;

n is 0, 1, or 2;

q is 22, 23, 26, 27, 28, 29, 32, 33, or 34;

comprising

- reacting a compound of formula 33a: